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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,562	10/11/2005	Ljubomir Antoncic	16580.0006FPWO	2564
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MERCHANT & GOULD PC				
P.O. BOX 2903				
MINNEAPOLIS, MN 55402-0903				
EXAMINER				
LOEWY, SUN JAE Y				
ART UNIT		PAPER NUMBER		
1626				
MAIL DATE		DELIVERY MODE		
09/24/2010		PAPER		

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.



### Office Action Summary

**Application No.**

10/552,562

**Applicant(s)**

ANTONCIC ET AL.

**Examiner**

SUN JAE Y. LOEWE

**Art Unit**

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 06 July 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 11, 12, 22, 23, 26-29 and 31-33 is/are pending in the application.
- 4a) Of the above claim(s) 32 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11, 12, 22, 23, 26-29, 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_



## **DETAILED ACTION**

### ***Response to Amendment***

1. The amendments to the claims filed on July 6, 2010 have been fully considered. The 35 USC 112 1<sup>st</sup> paragraph rejection is maintained. Applicant's arguments are considered. However, it is noted that the predictability in the field of making crystalline/amorphous forms of atorvastatin is unpredictable. A new 35 USC 112 1<sup>st</sup> paragraph rejection addressing this point is made herein. It is suggested for Applicant to narrow the scope of the claims to diisopropyl ether.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.



The breadth of the claims

A method of preparing amorphous atorvastatin.

The nature of the invention

The claimed invention is a "generic" process for making amorphous material.

The state of the prior art/level of ordinary skill/level of predictability

The state of the art for preparing solid forms of any given compound is unpredictable (eg. see Chawla et al., p. 9, 1st and 2nd paragraphs):

- The number or existence of solid forms cannot be predicted.
- The more diligently any system is studied the larger the number of polymorphs discovered
- It is not commonly known in the art, or predictable, how different solid forms are made (Newman et al., p. 898, 2<sup>nd</sup> column, last paragraph).

Evidence indicates that, to date, a high level of unpredictability exists in the art for preparing solid forms (including amorphous) of atorvastatin. See representative disclosure of Finkelstein et al. (WO 2006/037125), excerpts below:



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Crystalline form	Mediums of crystallization
Amorphous	Ethyl acetate-Hexane (Eumecolipolite or cyclic or branched Hydrocarbon)
Amorphous	Acetone Acetonitrile
Amorphous	THF-Toluene
Form I	Misc. of MTBE, Diethyl ether
Form II	MeOH/water
Form IV	1-Hexanol EtOH/water MeOH
Form V	EtOH/water
Form VI	Acetone/water
Form VII	EtOH
Form VIII	EtOH, MeOH/water EtOH 1-Hexanol/water IPA/water
Form IX	1-Hexanol 1-Hexanol-Hexane 1-Hexanol/PPA 1-Hexanol/water EtOH 1-Hexanol/EtOH
Form X	EtOH/water
Form XI	NEC IPA
Form XII	EtOH/water

The following is noted (MPEP 2164.03):

in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art.

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is

The amount of direction provided by the inventor/existence of working examples



The working examples provided by the instant specification are limited to the process of making amorphous atorvastatin using diisopropyl ether.

MPEP 2164.02 states (excerpts below):

The presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims.

Furthermore, due to the unpredictability in the art for preparing solid form (including amorphous) of atorvastatin, one of ordinary skill would not be able to predict what solvents would lead to the amorphous form. One of ordinary skill would not be able to extrapolate the working examples provided to the claimed invention.

*The quantity of experimentation needed to make or use the invention*

MPEP 2164.01(a) states:

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Based on the evidence regarding each of the above factors (see discussion above), the specification, at the time the application was filed, would not have



taught one of ordinary skill in the art how to practice the claimed invention without undue experimentation.

The instant claims *prima facie* lack enablement.

### ***Conclusion***

3. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUN JAE Y. LOEWE whose telephone number is (571)272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Sun Jae Y. Loewe/  
9-10-2010